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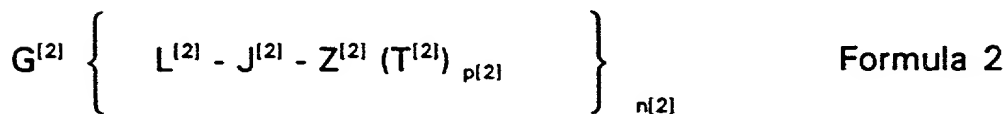
Claims

WE CLAIM:

1. A conjugate comprising (a) biological or chemical molecules reacted with (b) a chemically-defined, non-polymeric valency platform molecule of the formula:



or



wherein

each of  $G^{[1]}$  and  $G^{[2]}$ , if present, is independently a linear, branched or multiply-branched chain comprising 1-2000 chain atoms selected from the group C, N, O, Si, P and S;

each of the  $n^{[1]}$  moieties shown as  $T^{[1]}$  and each of the  $p^{[2]} \times n^{[2]}$  moieties shown as  $T^{[2]}$  is independently chosen from the group  $NHR^{SUB}$  (amine),  $C(=O)NHNHR^{SUB}$  (hydrazide),  $NHNHR^{SUB}$  (hydrazine),  $C(=O)OH$  (carboxylic acid),  $C(=O)OR^{ESTER}$  (activated ester),  $C(=O)OC(=O)R^B$  (anhydride),  $C(=O)X$  (acid halide),  $S(=O)_2X$  (sulfonyl halide),  $C(=NR^{SUB})OR^{SUB}$  (imide ester),  $NCO$  (isocyanate),  $NCS$  (isothiocyanate),  $OC(=O)X$  (haloformate),  $C(=O)OC(=NR^{SUB})NHR^{SUB}$  (carbodiimide adduct),  $C(=O)H$

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(aldehyde),  $C(=O)R^B$  (ketone), SH (sulfhydryl or thiol),  
OH (alcohol),  $C(=O)CH_2X$  (haloacetyl),  $R^{ALK}X$  (alkyl  
halide),  $S(=O)_2OR^{ALK}X$  (alkyl sulfonate),  $NR^1R^2$  wherein  $R^1R^2$   
5 is  $-C(=O)CH=CHC(=O)-$  (maleimide),  $C(=O)CR^B=CR^B_2$  ( $\alpha,\beta$ -  
unsaturated carbonyl),  $R^{ALK}-Hg-X$  (alkyl mercurial), and  
 $S(=O)CR^B=CR^B_2$  ( $\alpha,\beta$ -unsaturated sulfone);  
wherein

each X is independently a halogen of atomic number  
10 greater than 16 and less than 54 or other good leaving  
group;

each  $R^{ALK}$  is independently a linear, branched, or  
cyclic alkyl (1-20C) group;

each  $R^{SUB}$  is independently H, linear, branched, or  
15 cyclic alkyl (1-20C), aryl (6-20C), or alkaryl (7-30C);

each  $R^{ESTER}$  is independently N-hydroxysuccinimidyl,  
p-nitrophenoxy, pentafluorophenoxy, or other activating  
group;

each  $R^B$  is independently a radical comprising 1-50  
20 atoms selected from the group C, H, N, O, Si, P and S;

each of the  $n^{[2]}$  moieties shown as  $L^{[2]}$ , if present, is  
independently chosen from the group O,  $NR^{SUB}$  and S;

each of the  $n^{[2]}$  moieties shown as  $J^{[2]}$ , if present, is  
independently chosen from the group  $C(=O)$  and  $C(=S)$ ;

25  $n^{[1]} = 1$  to 32;

$n^{[2]} = 1$  to 32;

$p^{[2]} = 1$  to 8;

with the proviso that the product  $n^{[2]} \times p^{[2]}$  be  
greater than 1 and less than 33;

30 each of the  $n^{[2]}$  moieties shown as  $Z^{[2]}$  is  
independently a radical comprising 1-200 atoms selected  
from the group C, H, N, O, Si, P and S, containing

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attachment sites for at least p<sup>[2]</sup> functional groups on alkyl, alkenyl, or aromatic carbon atoms.

5           2. A conjugate according to claim 1, wherein the  
biological molecules comprise polynucleotide duplexes of  
at least about 20 base pairs each bound to the valency  
platform molecule, the duplexes each having a significant  
binding activity for human systemic lupus erythematosus  
10 anti-dsDNA autoantibodies.

3. A conjugate according to claim 1, wherein the  
biological or chemical molecules are selected from the  
group consisting of carbohydrates, lipid,  
15 lipopolysaccharides, peptides, proteins, glycoproteins,  
single-stranded or double-stranded oligonucleotides,  
haptens, or chemical analogs thereof such as mimotopes,  
aptamers.

20           4. A conjugate according to claim 1, wherein the  
biological or chemical molecules are analogs of  
immunogens wherein (a) the analog binds specifically to B  
cells to which the immunogen binds specifically and (b)  
the conjugate lacks a T cell epitope.

25           5. The conjugate of claim 1, wherein the valency  
platform molecule is derivatized by a reagent selected  
from the group consisting of DABA, BAHA, BAHA<sub>ox</sub>, and AHAB.

30           6. The conjugate of claim 2, wherein a linker  
molecule couples the duplexes to the valency platform  
molecule.

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7. The conjugate of claim 6, wherein the linker molecule is selected from the group consisting of HAD and HAD<sub>p</sub>S.

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8. The conjugate of claim 2, wherein the duplexes are substantially homogeneous in length.

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9. The conjugate of claim 2, wherein the duplexes are substantially homogeneous in nucleotide composition.

10. The conjugate of claim 2, wherein the duplexes are 20 to 50 bp in length.

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11. The conjugate of claim 2, wherein the duplexes are bound to the valency platform molecule at or proximate one of their ends.

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12. The conjugate of claim 2, wherein the conjugate is a tolerogen for human systemic lupus erythematosus.

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13. A conjugate according to claim 2, wherein the polynucleotide duplexes have a B-DNA type helical structure and a significant binding activity for human systemic lupus erythematosus anti-dsDNA autoantibodies.

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14. A pharmaceutical composition for treating lupus comprising the conjugate of claim 2 formulated with a pharmaceutically acceptable injectable vehicle.

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15. A method for treating an individual for lupus comprising administering a therapeutically effective amount of the composition claim 14 to an individual in need of such treatment.

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16. A method for making the conjugate of claim 2, comprising:

5 (a) bonding a multiplicity of single-stranded polynucleotides of at least about 20 base pairs each on the valency platform molecule; and

10 (b) annealing complementary single-stranded polynucleotides to the single-stranded polynucleotides conjugated to the valency platform molecule to form said duplexes.

15 17. A pharmaceutical composition for treating an antibody-mediated pathology comprising a therapeutically effective amount of the conjugate of claim 2, combined with a pharmaceutically acceptable carrier.

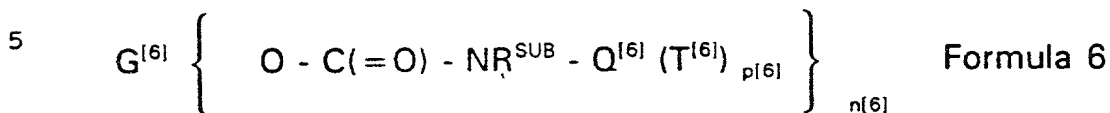
20 18. A method of inducing specific B cell anergy to an immunogen in an individual comprising administering to the individual an effective amount of the conjugate of claim 17.

25 19. A method of treating an individual for an antibody-mediated pathology in which undesired antibodies are produced in response to an immunogen comprising administering a therapeutically effective amount of the conjugate of claim 17 to the individual.

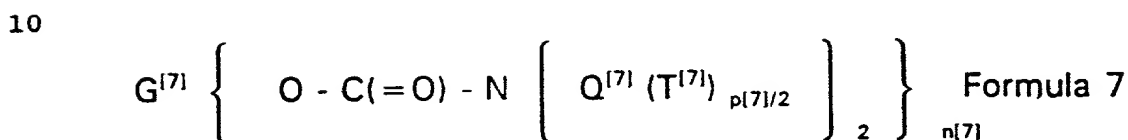
30 20. A method for making a conjugate according to claim 2, comprising  
(a) covalently bonding the analog of the immunogen lacking T cell epitopes to the chemically-defined valency platform molecule to form a conjugate; and  
35 (b) recovering the conjugate from the reaction mixture.

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21. A chemically-defined, non-polymeric valency platform molecule of the formula:



or



wherein

each of  $G^{[6]}$  and  $G^{[7]}$ , if present, is independently a linear, branched or multiply-branched chain comprising 1-2000 chain atoms selected from the group C, N, O, Si, P and S;

each of the  $n^{[6]} \times p^{[6]}$  moieties shown as  $T^{[6]}$  and each of the  $n^{[7]} \times p^{[7]}$  moieties shown as  $T^{[7]}$  is independently chosen from the group

$NHR^{SUB}$  (amine),  $C(=O)NHNHR^{SUB}$  (hydrazide),  $NHNHR^{SUB}$  (hydrazine),  $C(=O)OH$  (carboxylic acid),  $C(=O)OR^{ESTER}$  (activated ester),  $C(=O)OC(=O)R^B$  (anhydride),  $C(=O)X$  (acid halide),  $S(=O)_2X$  (sulfonyl halide),  $C(=NR^{SUB})OR^{SUB}$  (imide ester),  $NCO$  (isocyanate),  $NCS$  (isothiocyanate),  $OC(=O)X$  (haloformate),  $C(=O)OC(=NR^{SUB})NHR^{SUB}$  (carbodiimide adduct),  $C(=O)H$  (aldehyde),  $C(=O)R^B$  (ketone),  $SH$  (sulfhydryl or thiol),  $OH$  (alcohol),  $C(=O)CH_2X$  (haloacetyl),  $R^{ALK}X$  (alkyl halide),  $S(=O)_2OR^{ALK}X$  (alkyl sulfonate),  $NR^1R^2$  wherein  $R^1R^2$  is  $-C(=O)CH=CHC(=O)-$  (maleimide),  $C(=O)CR^B=CR^B$ , ( $\alpha,\beta$ -unsaturated carbonyl),

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$R^{ALK}-Hg-X$  (alkyl mercurial), and  $S(=O)CR^B=CR^B_2$  ( $\alpha,\beta$ -unsaturated sulfone);  
wherein

5        each X is independently a halogen of atomic number greater than 16 and less than 54 or other good leaving group;

         each  $R^{ALK}$  is independently a linear, branched, or cyclic alkyl (1-20C) group;

10        each  $R^{SUB}$  is independently H, linear, branched, or cyclic alkyl (1-20C), aryl (1-20C), or alkaryl (1-30C);

         each  $R^{ESTER}$  is independently N-hydroxysuccinimidyl, p-nitrophenoxy, pentafluorophenoxy, or other activating group;

15        each  $R^B$  is independently a radical comprising 1-50 atoms selected from the group C, H, N, O, Si, P and S;

$n^{[6]} = 1$  to 32;

$p^{[6]} = 1$  to 8;

20        with the proviso that the product  $n^{[6]} \times p^{[6]}$  be greater than 1 and less than 33;

$n^{[7]} = 1$  to 32;

$p^{[7]} = 2, 4, 6$  or 8;

         with the proviso that the product  $n^{[7]} \times p^{[7]}$  be greater than 1 and less than 33;

25        each of the  $n^{[6]}$  moieties shown as  $Q^{[6]}$  and each of the  $2 \times n^{[7]}$  moieties shown as  $Q^{[7]}$  is independently a radical comprising 1-100 atoms selected from the group C, H, N, O, Si, P and S, containing attachment sites for at least  $p^{[6]}$  (for  $Q^{[6]}$ ) or  $p^{[7]}/2$  (for  $Q^{[7]}$ , where  $p^{[7]}/2$  is an integer)  
30        functional groups on alkyl, alkenyl, or aromatic carbon atoms.

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